REMARKS

The Final Office action dated April 19, 2010 is acknowledged. Claims 1-24 are pending in the instant application. Claims 7-15, 18-20 and 23-24 have been rejected and claims 1-6, 16, 17, 21 and 22 have been withdrawn. Reconsideration is respectfully requested in light of the arguments made herein. No new matter has been added.

Rejection of claim 7 under 35 U.S.C. 102(b)

Claim 7 has been rejected under 35 U.S.C. 102(b) as being anticipated by Vonin, et al. (Stvo Meditsina; Moscow, Russia; Vol. 91, No. 2 (Feb. 1991), pages 111-115). The Examiner states that the Vonin, et al. reference teaches the treatment of schizophrenic patients with deoxypeganine (Abstract; and page 115).

The Applicants still strongly disagree with the Examiner's conclusion and submit that the present invention as defined in the present claims is patentably distinct from the invention disclosed in the prior art Vonin, et al. reference.

The Applicants respectfully submit that schizophrenic psychosis, along with its specific symptoms, is a disease that is fundamentally different from schizophrenia that is accompanied by well-defined symptoms. In particular, the presently claimed invention is directed to the use of deoxypeganine, or a derivative of deoxypeganine, as long as the derivative is simultaneously an inhibitor of acetylcholine esterase and of monoamine oxidase for treating a schizophrenic psychosis which is connected with at least one of increased monoamine oxidase and decreased functionality of nicotinic acetylcholine receptors.

Schizophrenic psychosis is characterized by distortion of reality and disturbances of thought and language, as well as withdrawal from social contacts. Fundamental

symptoms of schizophrenic psychosis are the blocking of thought processes, disorders of emotional life (affect) and drive, loss of reality (autism) and the so called "ego disorder" which is understood to mean the split experience of one's own personality (see paragraph [00005] in the present specification).

In contrast to the disclosure of the presently claimed invention, Vovin, et al. fail to teach or describe the treatment of schizophrenic psychosis nor any of its symptoms. The Vovin, et al. reference is directed to the treatment of a different class of deficitary symptoms that are classified as apathoabulic symptoms, along with a reduced circulation of acetylcholine which is the basic mediator of motor activity (page 3, second paragraph of Vovin, et al.). Accordingly, apathoabulic symptoms are related to deficiencies in the motor activity, such as vital tonus, absent initiative, emotional detachment with quantitatively and qualitatively impoverished speech (page 3, paragraph 6 of Vonin, et al.).

In summary, the reference of Vovin, et al. is related to the treatment of apathoabulic symptoms which are totally different from the symptoms ensuing from schizophrenic psychosis of the presently claimed invention. Consequently, the disclosure of Vovin, et al. simply cannot anticipate the presently claimed invention. In this respect, the Applicants respectfully disagree with the Examiner's assertion that the symptoms decreased or absent initiative and emotional detachment which belong to the apathoabulic manifestation of schizophrenia are in line with the Applicant's description of symptoms of schizophrenic psychosis. The text of the present application merely refers to disorders of emotional life and drive. However, a disorder of drive is not equivalent to absent initiative because a disorder of drive can also include any type of hyperactivity, which is

the total opposite of absent initiative.

The fact that the symptoms of schizophrenic psychosis are fundamentally distinguished from the apathoabulic manifestation of schizophrenia is also reflected in the causes of an action underlying these deficiencies. It is thus submitted that present claim 7 clearly and unambiguously recites that schizophrenic psychosis is related to increased monoamine oxidase activity or decreased functionality of nicotinic acetylcholine receptors. In other words, schizophrenic psychosis is mainly affected by increased monoamine oxidase activity or decreased functionality of nicotinic acetylcholine receptors.

According to the disclosure of Vovin, et al., the apathoabulic manifestation of schizophrenia results from an inadequacy of adrenergic mechanism along with the reduced circulation of acetylcholine. Accordingly, the apathoabulic manifestation of schizophrenia is related to deficiencies in the presence of acetylcholine, but not to any activity of increased monoamine oxidase or decreased functionality of nicotinic acetylcholine receptors, because these enzymes and receptors, receptively, do not directly interfere with the presence of acetylcholine.

As the reference of Vovin, et al. does not disclose any kind of schizophrenic deficiencies that are connected with either increased monoamine oxidase activity or decreased functionality of nicotinic acetylcholine receptors, the subject matter of claim 7 is novel in view of Vovin, et al. In summary, the subject matter of the presently claimed invention is not anticipated by Vovin, et al. since the reference does not teach or disclose the treatment of schizophrenic psychosis being associated with an increased activity of monoamine oxidase and/or reduced functionality of nicotinic acetylcholine receptors.

In conclusion, it is submitted that Vonin, et al. fail to teach each and every limitation of the present claims, and therefore fail to anticipate the present invention as set forth in the present claims. Withdrawal of this rejection is respectfully requested.

Rejection of claims 8-15, 18-20 and 23-24 under 35 U.S.C. 103(a)

Claims 8-15, 18-20 and 23-24 have been rejected as being unpatentable over Vonin, et al., as applied to claim 7, and in view of U.S. Publication No. 2004/0132751 (Opitz, et al.) The Examiner argues that Vonin, et al. disclose the treatment of schizophrenic patients with deoxypeganine, but do not disclose a daily dose, the proportions of the active substance in a pharmaceutical or route of administration. The Examiner refers to Opitz, et al. for teaching the use of deoxypeganine for the treatment of disorders of CNS, including psychiatric symptoms and for teaching that deoxypeganine can be used in its free base form or as an acid addition salt, with the preferred salt being deoxypeganine hydrochloride and hydrobromide. The Examiner also argues that Opitz, et al. teach that deoxypeganine is administered in a pharmaceutical preparation which contains the agent in proportions of from 0.1 to 90% by weight calculated as free deoxypeganine and that the daily dose is in the range from 0.1 to 100 mg. The Examiner also states that it is taught that deoxypeganine can be administered orally, parenterally, as a depot medicament and transdermally. Lastly, the Examiner states that derivatives are structurally analogous to deoxypeganine and will have the same property of inhibiting both acetylcholinesterase and monoamine oxidase, absent a showing of unexpected results. Thus, the Examiner thus concludes that the combination of the teachings of Vonin, et al. and Opitz, et al. render the presently claimed invention obvious and unpatentable.

It is respectfully submitted that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. The Applicants respectfully submit that one skilled in the art would have no suggestion or motivation to combine the aforementioned references in order to arrive at the present invention. Additionally, even if one skilled in the art were to consider the teachings of the cited prior art alone or in combination, each and every limitation of the present invention would not be disclosed, nor would there be a reasonable expectation of success if the aforementioned references were to be considered.

The Applicants first respectfully disagree with the Examiner's position for at least the numerous deficiencies of Vonin, et al. set forth above. Optiz, et al. fail to make up for any of the deficiencies of Vonin, et al. In particular, it is submitted that for assessing the obviousness of the subject matter in view of Vovin, et al., it is essential to know whether schizophrenia accompanied by apathoabulic symptoms pertains to schizophrenic psychosis that is associated with an increased activity of monoamine oxidase and/or impaired functionality of nicotinic acetylcholine receptors. However, this is strongly not the case as can be shown, for example, from an article by Gamaleia, N.B. (Zh Nevropatrol Psikhiatr Im SS Korsakova; 1982; 81(5), pages 700-708 – the English summary of which is enclosed). Gamaleia discloses that 17 out of 25 patients suffering from a schizophrenia psychosis, and 5 of which were suffering from an apathoabulic type of schizophrenia had an impaired monoamine metabolism which could be due to an

insufficient efficacy of the enzymes of dopamine catabolism. Catabolism designates the enzymatic reactions that mediate degradation of organic compounds. Dopamine is degraded by a monoamine oxidase. The lowering of the homovanillic acid to dopamine ratio in those 17 patients shows that the function of monoamine oxidase is impaired in these patients, because an increase in dopamine results from a low monoamine oxidase activity. Thus, schizophrenia accompanied by apathoabulic symptoms does not belong to a class of schizophrenic psychosis being associated with an increased activity of monoamine oxidase.

Accordingly, for a medical treatment of schizophrenia being accompanied with apathoabulic symptoms, it would be advised to enhance dopamine catabolism, for example by improving activity of monoamine oxidase. However, those skilled in the art know that deoxypeganine inhibits the monoamine oxidase. In this regard, it is noted that deoxypeganine differs from galanthamine. Thus, one skilled in the art would expect that administering deoxypeganine would impair the metabolism of monoamines in patients suffering from schizophrenia accompanied with apathoabulic symptoms and would thus amplify the schizophrenic symptoms. This would clearly keep the skilled artisan away from administering deoxypeganine to patients suffering from schizophrenia of the apathoabulic type.

In this regard, it is submitted that the reference of Vovin, et al. does not distinguish between patients that obtained deoxypeganine and patients that obtained galanthamine in combination with amycil when showing the results of their study. Thus, it is unclear whether deoxypeganine in combination with amycil was effective at all or whether the patients who received deoxypeganine belong to one of the groups that did not

display any effects or just negligible effects. It is submitted that a clear and unambiguous disclosure of the efficacy of deoxypeganine would be an indispensible requirement that that the teaching of Vovin, et al. could have rendered the use of deoxypeganine suffering from schizophrenic psychosis being associated with an increased activity of monoamine oxidase and/or reduced functionality of nicotinic acetylcholine receptors obvious to one skilled in the art.

Moreover, it also remains enigmatic whether the patients that were given deoxypeganine in combination with amycil belong to those patients that had undesired side effects. This uncertainty would rather prevent one skilled in the art to administer deoxypeganine for treating a schizophrenic psychosis than encourage him to do so. Accordingly, the disclosure of Vonin, et al. does not render obvious the use of deoxypeganine for manufacturing a medicament for the treatment of schizophrenic psychosis being associated with an increased activity of monoamine oxidase and/or reduced functionality of nicotinic acetylcholine receptors.

In view of the above, the combination of teachings of Vonin, et al. with Opitz, et al. fail to teach each and every limitation of the present claimed invention. Therefore, the Applicants respectfully request that this obviousness rejection be withdrawn.

Conclusion

For the foregoing reasons, it is believed that the present application, as amended, is in condition for allowance, and such action is earnestly solicited. Based on the foregoing arguments, amendments to the claims and deficiencies of the prior art references, the Applicants strongly urge that the obviousness-type rejection and anticipation rejections be withdrawn. The Examiner is invited to call the undersigned if

there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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